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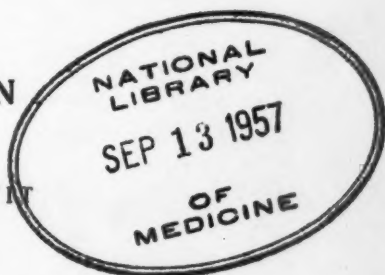
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OBSERVATIONS ON THE STRUCTURE OF THE
BRONCHIAL WALL IN BRONCHIECTASIS

BY

MARTTI TURUNEN, LARS HJELT, GUSTAF ELFVING
and TERHO MAAMIES

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HELSINKI 1957

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INTRODUCTION

Bronchiectasis is a pathological condition marked by dilatation of the bronchi, with chronic inflammations and destructive changes in the dilated bronchi and their walls. The pathogenesis of the disease has been the subject of different investigations for a considerable time. This is primarily due to the polyphase character of the disease and its different forms of manifestation.

Investigators are for the most of the opinion that bronchiectasis usually occurs following destructive changes in the bronchial walls brought about by inflammatory processes. Some workers emphasise the significance of the congenital structure of the bronchial walls and of mechanical factors, and ascribe less significance to inflammatory changes.

Attempts have been made to classify bronchiectasis into different groups on the basis of structural changes in the bronchial wall. Engel made a difference between two main groups: 1) Congenital cystic lung. 2) Acquired bronchiectasis. The latter group is divided into two further groups, the first consisting of bronchiectasis originating in so-called congenital bronchomalacia and the second of ectasis following acquired bronchomalacia. This last group, in other words, is formed particularly of bronchiectasis produced by inflammatory destruction.

The grouping of bronchiectasis proposed by Whitewell (1952) is very clear and serviceable in many respects. According to him, 4 types of bronchiectasis can be differentiated. He leaves so-called congenital bronchiectasis undescribed, mentioning that approximately 10 per cent of all cases belong to this group. Acquired ectasis is divided by him into 3 subgroups:

1. follicular bronchiectasis, with the most prominent microscopic finding of lymph tissue forming follicles in the bronchial wall.

2. saccular bronchiectasis, marked by pocket-like formations in the bronchi and by metaplastic changes of the bronchial epithelium.

3. atelectatic bronchiectasis, which is a very heterogeneous group. It is characterised by bronchial dilatation and lobular or segmental atelectasis.

It can be seen that opinions vary concerning the histological structure of the bronchial wall in bronchiectasis. *E.g.* Lisa and Rosenblatt (1943) stated on the basis of 110 cases investigated post mortem, that the bronchial elastic tissues were relatively unimpaired, whereas Whitewell maintains in his paper, that the first and most persistent changes are just destruction of the elastic tissue.

Similar conflicting opinions can be found in the literature, they are partly due to the circumstances that numerous investigators have examined changes occurring in some particular tissue, disregarding changes in the total structure of the bronchial wall. We therefore felt justified in examining a number of bronchiectatic lungs and in comparing the bronchial wall structures found in them to the structure of lungs which were considered normal.

It was not our endeavour to collect as extensive a series as possible, we decided instead to keep to typical cases and to clarify:

- I The relation between age and type of bronchiectasis.
- II The reaction of elastic tissue in different types of bronchiectasis.
- III Changes in the other supporting tissues and glands of the bronchial walls in different types of bronchiectasis.
- IV Whether the mechanism of origin can be estimated on the basis of the histological picture.

MATERIAL AND METHODS

A study was made of 17 patients of the former First and present Third Surgical Clinic, all of whom had been operated upon for bronchiectasis. For them we had at our disposal their preliminary history and clinical status with radiological findings, as well as findings at operation and the excised diseased lung or a portion of it. In 12 cases no pathological changes, apart from bronchiectasis, could be found in the lungs. Five patients had in addition pulmonary tuberculosis, for which they had been treated previously. In two of these cases the patient had got a foreign body into his lungs when he was a child. Operation revealed in both patients a corn ear in the posterobasal bronchus of the right lower lobe.










All cases with surgical treatment were comparatively young persons; we therefore collected a post mortem material comprising 34 bronchiectatic patients. We also had as control material 18 lung samples which were collected from autopsy material. In these cases autopsy had been performed 24 hours after death, and the lungs were considered normal. In all the groups of this series specimens for the histological study were taken in different bronchial degrees and also in parenchyma. Samples were also taken particularly in areas bordering on extensive ectatic bronchi, in order to study changes in the bronchioli. Fixation of all the specimens was carried out with 10 per cent formaldehyde, after which they were soaked in paraffin. The 5 my thick sections were stained with Weigert's resorcin-fuchsin to bring out the elastic tissues, and for a general estimation with hematoxylin-eosin and Weigert-van Gieson.

The patients were grouped according to the classification of Whitewell. The surgical series with more important clinical information is presented on Table 1. The results from the post mortem material are shown on Table 2. The normal series has not been tabulated in detail, instead, it was used in the course of the investigation as control material.









RESULTS

Table 1 shows that among the patients operated on, 10 were women and 7 men. Cases 5 and 14 approximately represent the congenital type, the others fall into the groups of acquired bronchiectasis.

TABLE 1.

No.	Age	Sex	History					Status	Therapy	Recov- ery	Histolo- gic. type
			Duration	Fever	Sputum	tb	corp. alien.				
1.	19 y.	♀	circa 15 y.	++	++	—	+		Ectomy of the lower and middle lobe of the right lung	Good	Follicular
2.	34 y.	♀	circa 3 y.	+	+	—	—		Ectomy of the right upper lobe and resection of the apical seg- ment of the right lower lobe	Good	Saccular
3.	40 y.	♀	circa 4 y.	+	+	+	—		Pneumonectomy on the left side	Good	Saccular
4.	7 y.	♀	circa 3 y.	+++	+	—	—		Pneumonectomy on the left side	Good	Follicular
5.	1 y. 2 m.	♂	1 y. 2 m.	+++	+	—	—		Ectomy of the right upper lobe	Good	Congen- ital
6.	31 y.	♂	7 y.	+	—	—	—		Pneumonectomy on the left side	Good	Saccular
7.	18 y.	♀	17 y.	+	+++	—	—		Ectomy of the left lower lobe and lingulectomy	Good	Follicular
8.	28 y.	♂	10 y.	++	+++	—	—		Ectomy of the left lower lobe and lingulectomy	Good	Saccular
9.	18 y.	♀	6 y.	+	+	+	—		Pneumonectomy on the left side	Good	Follicular

Conten.

Histologic type	No.	Age	Sex	History					Status	Therapy	Recovery	Histologic type
				Duration	Fever	Sputum	tb	corp. alien.				
follicular	10.	48 y.	♂	10 y.	+	+	+	—		Pneumonectomy on the left side	Good	Atelectatic
saccular	11.	43 y.	♂	12 y.	+	+	+	—		Ectomy of the right upper lobe	Good	Atelectatic
saccular	12.	40 y.	♀	5 y.	+	++	—	—		Ectomy of the left lobe and lingulectomy	Good	Atelectatic
follicular	13.	21 y.	♀	circa 5 y.	++	+	—	—		Ectomy of the left lower lobe and lingulectomy	Good	Follicular
congenital	14.	13 y.	♀	6—7 y.	++	++	—	—		Ectomy of the right upper lobe	Good	Congenital
saccular	15.	34 y.	♀	4 y.	++	+	+	—		Pneumonectomy on the right side	Good	Saccular
follicular	16.	35 y.	♂	3—4 y.	+	++	—	—		Ectomy of the left lower lobe and lingulectomy	Good	Saccular
saccular	17.	9 y.	♂	2 y.	+++	+	—	+		Ectomy of the left lower lobe	Good	Follicular

The acquired types are distributed as follows: 6 follicular, 6 saccular and 3 atelectatic. In the follicular type the age range of the patients was 7 to 21 years, and the duration of the disease from 3 to 17 years. All were marked by feverishness and recurring inflammations of the respiratory tract. Expectations were copious in all. An interesting observation was case 1, in which the patient had previously got a corn ear into the lungs. Two cases had a history of whooping cough and one of measles, after which there had been an onset of symptoms. In 4 cases the left lower lobe was more seriously affected. In all these cases there was also involvement of the lingula. In the saccular type the age varied between 28 and 40 years. Of them 4 were in the region of the left lung and 2 in the right.

There were three atelectatic types. All gave a history of tuberculosis, on account of which they had been under treatment. Thoracoplasty was obviously also of significance, since it had been performed on two.

Table 2 illustrates the composition of the autopsy material. Four cases, which could not be classified are not included.

TABLE 2

	Follicular	Saccular	Atelectatic	Total
Men ..	5	9	5	19
Women	4	3	4	11

The age range of the follicular group was from 10 months to 21 years, in the saccular from 39 years to 79 years. One case in the saccular group had tuberculosis. Nine cases belonged to the atelectatic type. All these cases revealed changes in the mediastinal glands and in two cases thoracoplasty was performed. The age varied between 20 and 79 years.

In order to present a more detailed picture of the structure in different types, we shall describe some typical cases with their roentgenograms and their histological findings.

Case 5. — A male infant 14 months old who had always had a poor development. From the age of six months the patient had been affected with recurring slight respiratory infections. On admission it was found that the respiratory sound in the right upper region was not heard and

increased percussion resonance was present. Roentgenological examination revealed an extensive cystic formation in the region of the right upper lobe. Cystic cavities were found even elsewhere in the lobe. Excision of the right upper lobe was performed.

Pathological Report. — The specimen consisted of the right upper pulmonary lobe, which was almost completely filled by a thin-walled cyst. The cavity was aerated. No pus was present. Fairly small cystic bronchi were seen in the tissue surrounding the cystic wall. The cystic cavities were covered by low cuboidal epithelium (Fig. 1). Below the epithelium there was a thin layer of smooth muscle fibres and collagenous connective tissue. Some scarce mucous glands were seen in the collagenous tissue. No islets of cartilage could be found in the walls of cystic cavity. In some places of the walls was seen, acute inflammation with organisation of the surrounding lung tissue.

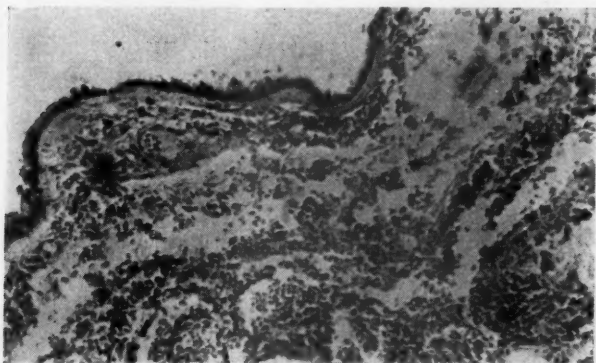


Fig. 1. — Wall of the cystic cavity lined by low cuboidal epithelium. Slight inflammatory cell infiltration is seen in the wall (Case 5).

Case 1. — A boy of 7 years, who at the age of 3 had had whooping cough. This was followed by several pneumonias. Radiological examination disclosed bronchiectasis, which was localised to the right lower lobe (Fig. 2). The patient was subjected to excision of the right lower lobe.

Pathological Report. — The tissue in the region of the excised lower lobe was solid, almost airless. The bronchi on the cross-section were thick-walled and dilated, pus was present in their cavities. Ectatic bronchi were surrounded by a process of interstitial pneumonia. It was seen in the microscopic preparations that the bronchial epithelium was fairly well preserved. In some places, however, there was epithelial ulceration but no squamous metaplasia. The bronchial walls were extremely thick. In the sub-epithelial tissues there were strong congestion, oedema and accumulations of inflammatory cells. Around the peripheral bronchi, sub-epithelially and in even deeper layers, plasma cell and lymphocyte accumulations were seen. They formed lymph follicles (Fig. 3). No elastic fibres

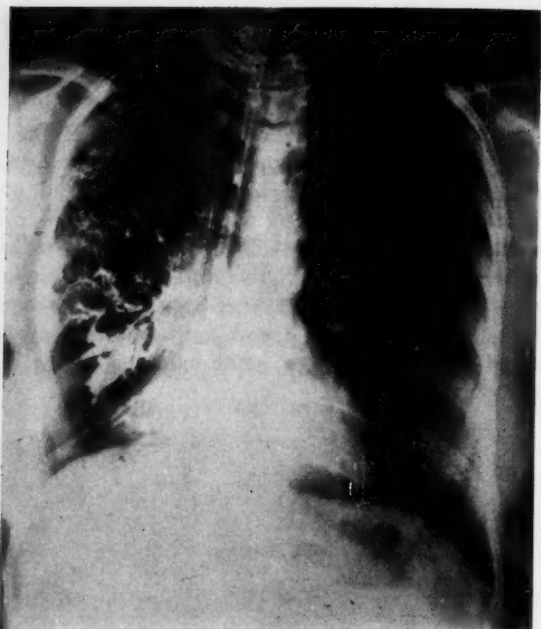


Fig. 2. — Radiological examination disclosed bronchiectasis, which was localised to the right lower lobe (Case 1).

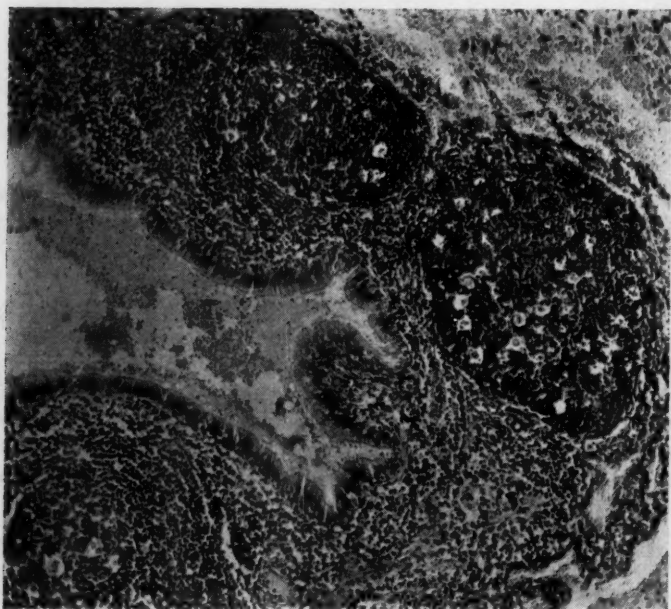


Fig. 3. — Lymph follicles in the wall of a peripheral bronchus (Case 1).

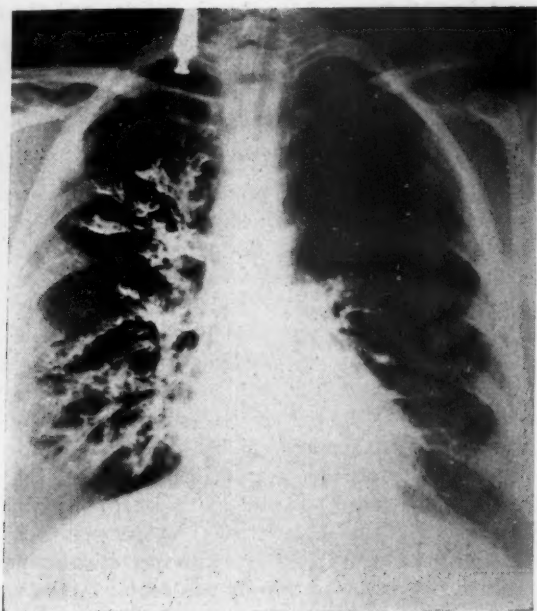


Fig. 4. — Bronchography demonstrated saccular bronchiectasis in the region of the right upper lobe and in the apical segment of the lower lobe (Case 2).



Fig. 5. — Polypous extrusions of the bronchial mucosa. Elastic tissue and muscle are well preserved (Case 2).

could be found in the areas of the lymph follicles and the muscle was fragmented. There was partial destruction of cartilages. The glandular excretory ducts were funnel-like. Granulation tissue continued into the surrounding pulmonary tissue as interstitial pneumonia. The bronchiolar walls had a strong inflammatory reaction. Lymph follicles were abundant. Elastic tissue as well as cartilage were nearly completely absent.

Case 2. — A woman aged 34, previously in good health, who had suffered from continual fever and cough for a couple of years. The symptoms continued to increase. The patient had abundant purulent sputum, which was sometimes mixed with blood. Bronchography demonstrated saccular bronchiectasis in the region of the right upper lobe and in the apical segment of the lower lobe (Fig. 4). Resection of the right upper lobe and of the apical segment of the lower lobe was performed on the patient.

Pathological Report. — The cut sections showed a shining pleura. The tissue was aerated. The main bronchi had normal dilatation, although their walls were thickened as compared with the normal. Their epithelium was hypertrophic and formed polypous extrusions. The peripheral bronchi formed sacks filled with pus. Under microscopical examination the main bronchus was seen to have an epithelium with formations of polypi (Fig. 5). Granulation tissue rich in blood vessels was found in the vicinity of the polypi. The granulation tissue was part of the diffuse inflammation of the bronchial wall. Elastic tissue, as well as muscle and cartilage were well preserved. The epithelium had a columnar character. The branches of segmental bronchi terminated in closed, sack-like formations (Fig. 6 a and b). They contained pus, and were lined with a uniform columnar epithelium which in places was transformed into the squamous variety. Below the epithelium there were aggregations of inflammatory cells and congestion. The wall was formed from connective tissue. Elastic tissue, muscle and cartilage were absent in the wall. In some places the peripheral branches were destroyed and fibrotic bands were seen in their stead. The surrounding pulmonary tissue was aerated.

Case 12. A woman of 40, who had suffered from tuberculosis for a time of 4 years. Bronchography showed a circular shadow in the region of the left upper lobe, calcified glands in the mediastinum and in the region of both lobes atelectasis and dilated bronchi (Fig. 7). Pneumonectomy of the left lung was performed on the patient.

Pathological Report. In the section the left main bronchus was strongly constricted and its mucous membrane was thick, hypertrophic. The peripheral bronchi were dilated and filled with pus. The histological sections showed in the vicinity of the lobular bronchus abundant tuberculous granulations, which in places penetrated close to the mucous membrane. Connective tissue formations were very abundant. In the thickened walls of the peripheral bronchial branches there were strong lymphocytic infiltrations (Fig. 8). The mucous membrane was transformed into squamous epithelium in extensive areas. The elastic tissue as well as the muscle were

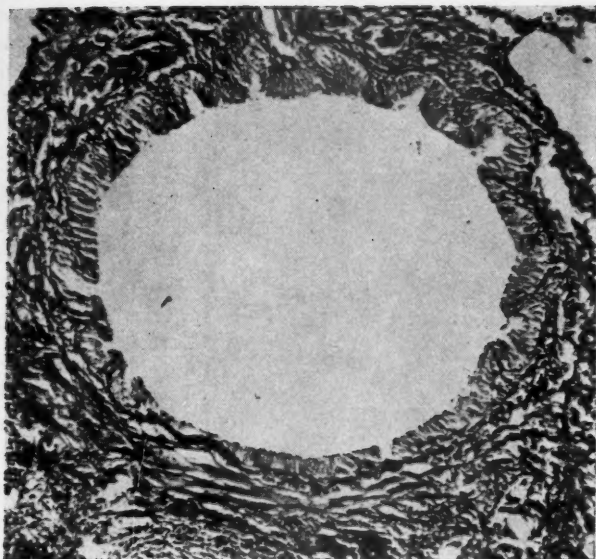


Fig. 6 a. — Saccule surrounded by collapsed lung tissue (Case 2).



Fig. 6 b. — Saccule lined by cuboidal low epithelium (Case 2).



Fig. 7. — Bronchography showed in the region of both lobes atelectasis and dilated brdnchi (Case 12).

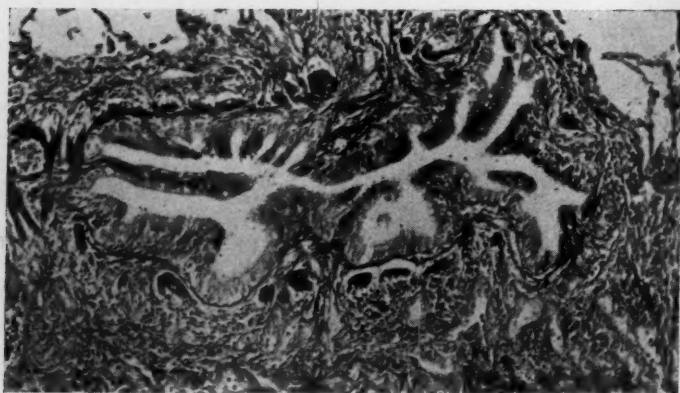


Fig. 8. — Thickened wall of a peripheral bronchus. Note the fragmentation of the elastic tissue and the lymphocytic infiltrations (Case 12).

almost completely destroyed. The cartilage on the other hand was better preserved. The alveoli were partly collapsed. Elastic tissue was absent in the alveolar walls. Their partitions were thick and fibrotic.

DISCUSSION

In spite of a great number of investigations on the subject, classification of bronchiectasis is still in its preliminary stage. The basis of classification generally applied is the shape of the dilated bronchus (Roles and Todd, Moll, Sicard and Forrestier). Confusion has been increased by the circumstance that some authors have used different denominations for similar lesions. A classification merely on the basis of shape is of minor significance from the point of view of etiology and pathogenesis. Some workers suggest in fact that the shape of the dilated bronchus depends on the type of the bronchus affected. (Moll, Fleischer).

Whitewell's classification is based on microscopic observations. He divided a series comprising 200 patients into four groups: congenital, follicular, saccular and atelectatic. We feel that this grouping is useful, even if a schematic division has the disadvantage that all cases do not fall within the sharply demarcated groups. We have nevertheless adhered to this classification in our study, even if 4 cases exhibited features belonging to the both two first groups, on account of which they have been left out of the classification. These cases belong to the autopsy material. Two cases of our series (case 5) fall into the category of congenital bronchiectasis. Both the clinical picture as well as radiological and microscopic findings are consistent with cases described in the literature (Moersch and Clagett, Ravitch and Hardy, Gross). The disease is a congenital developmental disorder, which is suggested in the first place by the absence of inflammatory and destructive changes. A further argument for poor primary development is the partial absence of bronchial cartilage in the walls of cystically dilated bronchi.

Cases belonging to the follicular and saccular types have as a rule clear histological criteria, and the history and age of the patients also provide indications of the type. In our series the age of patients with follicular bronchiectasis varied from 10 months to 21 year, the main part belonging to the younger age group, whereas saccular bronchiectasis generally affects older patients, usually past 20 years of age. In the group of follicular bronchiectasis the onset of disease

occurred in 3 cases after whooping cough and in one after measles. Obviously a virus infection possesses significance, because in this group interstitial pneumonia is part of the histological picture. Several authors have focused attention on this circumstance. The first change found in these cases was the destruction of the elastic tissue. It was fragmented or completely absent; particularly in such areas where lymph follicles were present. Lymph follicles also surrounded funnelshaped glandular passages and brought about in them a shape departing from the normal. Destruction of the muscle and cartilage was also found in connection with these follicles. The epithelium seemed to retain its columnar structure, nor could any metaplastic changes be demonstrated.

The saccular type was characterised by a formation of polypi on the mucous membrane of the main bronchus. Polypi produced abundant lumina. These polypi are probably due to subepithelial granulation tissue. The elastic tissue of the main bronchus was well preserved in spite of slight fragmentation, and so were the muscle and the cartilage. The ramifications of segmental bronchi terminated in closed pockets. The epithelium lining them was of the columnar or squamous variety. On the other hand, the elastic tissue, muscle and cartilage were completely absent in several places of the bronchi of this type. In more advanced forms these bronchi were totally destroyed and fibrotic bands or cystic formations were seen in their place, lined by cuboidal epithelium. The primary cause of saccular bronchiectasis is probably inflammation of medium size bronchi and destruction produced by it. The mechanical influence of pus in addition to inflammation of the mucous membrane, is probably of significance for the genesis. Reduction of the normal amount of bronchial ramifications described by Reid could be observed here.

In both the bronchiectatic types described above inflammatory changes and destruction of the walls are in the foreground. Highly divergent opinions can be found in the literature concerning the destruction of different parts of the walls. *E.g.* Duprez and Paulino state that destruction of the elastic tissue is the most common change, whereas Heppelstam maintains that it is well preserved in pulmonary fibrosis.

According to Whitewell's classification inflammatory changes vary in the histological picture of atelectatic bronchiectasis. In

some there is only superficial inflammation, thickening of the bronchial wall and replacement by collagenous connective tissue, in the absence of elastic tissue, muscle and cartilage. In other sections, again, moderate inflammation is seen in the bronchial wall, with resulting destruction of the connective tissue. In these cases marked epithelial metaplasia is seen in places. These cases were characterised by partial collapse of the pulmonary tissue around the bronchi and by the absence of inflammatory changes. It is further typical that several patients had simultaneous tuberculosis and enlarged mediastinal glands, or thoracoplasty had been performed on the patients. It is not easy to determine whether atelectasis was the primary cause of the bronchial changes in these cases. However, it seems obvious on the basis of *e.g.* case No. 12 that obstruction and atelectasis produced by tuberculosis were primary, and the changes in the bronchial wall secondary. Similar indications may also be found in the literature (Macpherson and Lutwyche, Brode).

The post mortem series was composed of patients mainly belonging to the older age groups. Obviously on account of this the saccular and atelectatic type was predominant among them. The histological changes in the bronchi were similar to those found in surgical series in the corresponding groups. In some autolysis had partly obliterated the mucous membrane and altered the staining ability of the tissue. Metaplastic changes in the mucous membranes were generally more abundant in the autopsy material than in the surgical series. Marked keratinisation was even found in some cases. Cell changes indicative of malignancy could not, however, be demonstrated.

SUMMARY

The study comprised 17 lung samples which were withdrawn from bronchiectasis patients in connection with surgery. Thirty four specimens were collected from the postmortem material of bronchiectasis patients, as well as 18 lungs of which neither gross nor microscopic examinations revealed any pathological changes. These latter lungs represent the control material of this study. Particular attention was focused on changes occurring in the wall of dilated bronchi. The lesions were grouped according to White-well's classification into cystic or congenital, follicular and atelectatic types.

The follicular form of bronchiectasis is a disease of the young, i.e. of persons under 20 years of age. It is marked by aggregation of lymphatic tissue in the diseased bronchial walls and by interstitial pneumonia. Saccular bronchiectasis is generally found in the older age groups. It is clearly distinguished from the follicular type by epithelial metaplasia and changes in the connective tissue. Interstitial inflammation does not occur in this form. The atelectatic type is characterised by at least a partial collapse of the surrounding lung tissue. The age range of persons affected with this type of the disease has a wide variation, and it is generally associated with pulmonary processes of different etiology. The process in the bronchial walls showed histological variations. The classification seems to be very serviceable, since only 4 cases had to remain outside, and they exhibited changes belonging both to the follicular and to the saccular type.

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